REMARKS

Claims 1-18 and 21-29 are currently pending in this application. Claims 1-18, 28, and 29 stand rejected under 35 U.S.C §§ 101, 112, first paragraph (written description and enablement), and/or 102. Claims 21-27 have been withdrawn as directed to non-elected subject matter.

REJECTION UNDER 35 U.S.C. § 101

Claims 1-18 and 21-29 stand rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter. The Examiner contends that "the recited claims do not require the transformation of an article or physical object to a different state."[1] Claims 1, 7, 13 and 28 have been amended to recite providing a sample containing a nucleic acid or protein from the human subject, detecting at least one 4G allele at the plasminogen activator inhibitor-1 (PAI-1) gene promoter site in the sample, and engaging the subject in exercise training. As such, the claims recite a transformation of an article or physical object to a different state because detecting the presence of at least one 4G allele at the PAI-1 gene promoter site in the sample would require transforming the sample. Engaging the subject in exercise training would further result in transformation in t-PA antigen and activity levels within the subject. Accordingly, withdrawal of this rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH, ENABLEMENT

Claims 1-18, 28, and 29 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.[2] The Examiner states that the specification enables two proposed claims.[3] Applicants have amended claims 1 and 28 to recite certain limitations suggested by the Examiner. However, Applicants have not amended these claims to recite "engaging the human subject in ***moderate exercise training***."

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[1] Office Action at page 3.

[2] Office Action at pages 6-14.

[3] Office Action at page 7.

The Examiner contends that "the nature of the invention requires knowledge of a period of time of exercise training sufficient to decrease the level of t-PA antigen (where any such decreased level of t-PA may prevent or ameliorate cardiovascular disease) or increase t-PA activity,"[4] but that "the specification provides no results from subjects that participated in extensive exercise, or subjects that were involved only in limited exercise."[5]

Applicants respectfully disagree that undue experimentation is necessary to verify that limited or extensive exercise would benefit the subject.

To determine if sufficient information is provided in the specification to enable a skilled artisan to make and use the claimed invention, one must inquire whether the claimed invention can be practiced by a skilled artisan without undue experimentation. MPEP § 2164.01. A large amount of experimentation would not be required to make and use the invention in the full scope as claimed. All that would be required is to repeat the experiments on subjects under limited and extensive exercise training protocols. This is not a large amount of experiments, and the experimental techniques are already described in the specification. Therefore, it is within the ability of one having ordinary skill to perform these experiments without undue burden on that person. Thus, claims 1-6, 28 and 29 are enabled by the specification.

The Examiner also contends that there is no indication that the invention would be effective in preventing the development of cardiovascular disease or alleviating symptoms of cardiovascular disease.[6]

Data directly showing improved fibrinolysis or alleviating symptoms of cardiovascular disease is not necessary because, as the specification recites, there is a link connecting t-PA activity and t-PA antigen levels with improved fibrinolysis (see specification at paragraphs [0012], [0024], and [0050]). There is also a link connecting improved fibrinolysis

[4] Office Action at page 8.

[5] Office Action at page 9.

[6] Office Action at page 9.

with alleviated symptoms of cardiovascular disease (see specification at paragraphs [0003] and [0007]).

The Examiner's contention that "there are in fact no results in the instant specification with regard to prevention of cardiovascular disease or amelioration of cardiovascular disease" is contrary to the statements contained within the specification. According to MPEP § 2107, the Examiner must accept statements of fact made by the applicant as true. By accepting these facts as true, since the specification provides data enabling a method of decreasing the level of tissue plasminogen activator (t-PA) antigen (claim 1), and enabling a method of increasing the level of tissue plasminogen activator (t-PA) activity (claim 28), it likewise provides data that fibrinolysis was improved and that symptoms of cardiovascular disease were alleviated in subjects with at least one 4G allele who engaged in exercise, because of the connection established in the specification between t-PA antigen levels, t-PA activity, fibrinolysis and cardiovascular disease. Thus, claims 7-18 are also enabled by the specification.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

REJECTION UNDER 35 U.S.C. § 102

Claims 1-18, 28, and 29 have been rejected under 35 U.S.C. § 102(b) as anticipated by Väisänen.[7]

I. THE RECITED INVENTION

Claims 1, 7, and 13 are directed to methods of decreasing the level of t-PA antigen; preventing cardiovascular disease; or ameliorating cardiovascular disease respectively. The methods comprise detecting at least one 4G allele at the plasminogen activator inhibitor-1 (PAI-1) gene promoter site in the subject, and engaging the subject in exercise training for a period of time sufficient to decrease the level of t-PA antigen. Claims 2-6 depend from claim 1. Claims 8-12 depend from claim 7. Claims 14-18 depend from claim 13. Claim 28 is directed to a

[7] Väisänen *et al.*, "Regular exercise, plasminogen activator inhibitor-1 (PAI-1) activity and 4G/5G promoter polymorphism in the PAI-1 gene," THROMB. HAEMOST (1999) 82: 1117-1120.

method of increasing the level of t-PA activity in a human subject. The method comprises detecting two 4G alleles at the plasminogen activator inhibitor-1 (PAI-1) gene promoter site in the human subject, and engaging the human subject in exercise training for a period of time sufficient to increase the level of t-PA activity. Claim 29 depends from claim 28.

In summary, the claims share the following common limitations – detecting at least one 4G allele genotype at the PAI-1 gene and engaging the subject in exercise.

II. THE CITED REFERENCES

Väisänen discloses identifying subjects having 4G/4G, 4G/5G, and 5G/5G genotypes.[8] Väisänen's research involved splitting one cohort into an exercise group and a reference group.[9] The study did not control for other genetic factors. For example, individuals within Väisänen's exercise group could have had other genetic factors not found in the reference group that distorted the results.

III. ARGUMENT

For a reference to anticipate a claimed invention, the reference must teach each and every limitation recited in the claim. Väisänen does not teach that placing a person with at least one 4G allele on an exercise regime will benefit that person more than a person who is homozygous 5G because there are too many uncontrolled variables in Väisänen's study.

Therefore, Väisänen does not anticipate the recited invention, and reconsideration and withdrawal of this rejection are respectfully requested.

[8] Väisänen at page 1118.

[9] Väisänen at page 1118

CONCLUSION

In view of the foregoing amendments to the claims and remarks, Applicants respectfully submit that the specification and claims are in condition for allowance. Accordingly, reconsideration and withdrawal of the asserted objections and rejections, and allowance of pending claims 1-18, 28, and 29, are respectfully requested. Rejoinder of withdrawn claims 21-27 is also requested.

Respectfully submitted,

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